Table III. Crystal Data

formula	$C_{22}H_{30}NO^+I^-$ (1)	$C_{22}H_{30}NO^+I^-$ (2)
fw	451.39	451.39
crystal size, mm	0.12 × 0.18 × 0.38	0.12 × 0.15 × 0.32
space group, Z	*Pnam*, 4	$P\bar{1}$, 4
cell (138 (2) K)		
a, Å	11.110 (7)	14.862 (9)
b, Å	11.098 (8)	15.124 (7)
c, Å	17.016 (13)	10.134 (4)
α, deg	90.0	96.67 (3)
β, deg	90.0	109.82 (3)
γ, deg	90.0	74.67 (4)
V, Å^3	2098.1	2065.8
cell (25 °C)		
a, Å	11.2105 (5)	14.877 (2)
b, Å	11.0650 (3)	15.464 (2)
c, Å	17.2148 (6)	10.182 (1)
α, deg	90.0	96.419 (8)
β, deg	90.0	109.942 (8)
γ, deg	90.0	75.128 (11)
V, Å^3	2135.4	2127.5
ρ_{obsd}, g cm^{-3} (25 °C)	1.399	1.401
ρ_{calcd}, g cm^{-3} (25 °C)	1.404	1.409
μ, cm^{-1}	14.15	14.37
no. of unique data	2227	8509
no. of obsd data ($I \geq 2\sigma(I)$)	1870	7037
R	0.028	0.028
R_w ($w = 1/\sigma(F)^2$)	0.036	0.032
N_v (parameters)	186	452
S (goodness of fit)	1.31	1.06
min/max esd in diff Fourier, e/Å^3	+0.56/−0.81	+0.56/−0.72

C(5)–C(4)–N(14) (115.0, 114.5°), C(4)–N(14)–C(16) (115.3, 115.2°), C(4)–C(5)–C(18) (119.6, 119.2°), and C(4)–C(3)–C(13) (120.7, 120.5°). There are more short intramolecular distances and presumably more strain in **2** than in **1**. In **2**, these short distances are between the methyl groups and hydrogen atoms on the ring and the methyl groups on the nitrogen atom.

The iodide atom in **1** is positionally disordered over two sites (90:10). The sites are only 0.362 Å apart, and for the remainder of this discussion, only the principally occupied site is used. In both compounds, the iodides interact with two *different* molecules. If the nitrogen atoms are considered as the center of tetrahedra with bonded carbons at the corners, then the iodide atoms interact with the nitrogen atoms through the C(15)–C(16)–C(17) face (A) and the C(4)–C(15)–C(16) face (B). In **1**, the I···N ($^1/_2 + x$, $^1/_2 - y$, z) distance through face A is 4.439 (2) Å and the I···N distance through face B is 4.447 (2) Å. In **2**, I(1) is bonded to molecule B through N($1 - x$, $1 - y$, $-z$) (face A; 4.620 Å) and N(x, $y - 1$, z) (face B; 4.485 (2) Å). Iodides I(2) and I(3) coordinate to molecule A through I(3)–N($x - 1$, y, $z - 1$) (face A; 4.471 (2) Å) and through I(2)–N($x - 1$, y, $z - 1$) (face B; 4.383 (2) Å).

In summary, the ^{1}H NMR data[1e] are consistent with a distorted molecule for both **1** and **2**, which are now demonstrated to exist as twist-boat forms in the solid state. Of course, in solution there may be rapidly equilibrating boat or pseudoboat forms present to minimize repulsive forces and to accommodate solvation parameters. The two examples reported herein are rare cases in this heterocyclic family.[3]

Experimental Section

General Procedures. Compounds **1** and **2** were prepared by the method reported[1e] and characterized. All NMR data have been recorded in Me_2SO-d_6[1e] on a Bruker WH 270 NMR spectrometer with a Bruker Model B-NC 12 data system (with a Nicolet NIC Model 294 disk memory coupler). The chemical shifts are in δ relative to internal $(H_3C)_4Si$. The values follow.

1: δ 1.46 [d, 6 H, CH_3(3,5), J = 7.0 Hz], 2.63–2.80 [m, 2 H, H(3,5)], 3.17 [s, 9 H, CH_3N], 4.03 [t, 1 H, H(4), J = 4.8 Hz, $w_{1/2}$ = 11.25 Hz], 4.61 [d, 2 H, H(2,6), J = 5.15 Hz], 7.34–7.62 [m, 10 H, ArH].

2: δ 1.23 [d, 6 H, CH_3(3,5), J = 7.0 Hz], 2.33–2.50 [m, 2 H, H(3,5)], 3.10 [s, 9 H, CH_3N], 3.73 [t, 1 H, H(4), J = 3.68 Hz, $w_{1/2}$ = 7.87 Hz] 4.40 [d, 2 H, H(2,6), J = 8.60 Hz], 7.31–7.51 [m, 10 H, ArH].

Crystallographic Experimental Data. Pertinent experimental details for the single-crystal diffraction studies of **1** and **2** are given in Table III. Intensity data at 138 (2) K for both compounds were collected on an Enraf-Nonius CAD-4 diffractometer equipped with a nitrogen-streaming, low-temperature device. Cell constants were determined by a least-squares fit to the $\pm 2\theta$ values of 48 intensity maxima distributed throughout reciprocal space. Density measurements were made by flotation in mixtures of hexane and in 1,1,2,2-tetrabromoethane. Structure **1** was solved by heavy-atom methods and refined by full-matrix, least-squares techniques.[4] Structure **2** was solved by the use of Patterson superposition methods. The occupancy of two iodine sites was determined from a difference Fourier and not further refined. Instead, the anisotropic thermal parameters of the major site and isotropic parameter for the minor site were refined. The least-squares refinement was blocked with one molecule in each block, while the iodine positions were included in both blocks. The hydrogen positions in both compounds were determined from difference Fouriers and refined with isotropic thermal parameters, while all other atoms were refined anisotropically. The bond distances involving hydrogen atoms varied between 0.92 and 1.08 Å in **1** and between 0.85 and 1.03 Å in compound **2**. The major residual peaks in the final difference Fourier were found to be close to the iodine positions.

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Supplementary Material Available: Tables of final atomic positional and thermal parameters (10 pages). Ordering information is given on any current masthead page.

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α-Arylation of Pyrrolidinones[1]

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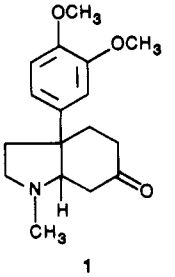
The total synthesis of alkaloids such as mesembrine (1) caused us to investigate the α-arylation of lactams, because



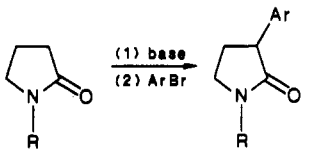
1

this is the first step of an efficient three-step mesembrine synthesis.[2] Alkylation of lactam and amide enolates is known,[3] but arylation is not common[4-8] because of the lack of both S_N2 and S_N1 reactivity of aryl halides.

The addition of nucleophiles to aryl halides can occur by three pathways—addition–elimination (via a Meisenheimer complex), elimination–addition (benzyne), or electron transfer (radical anion–radical).[9] The first of these routes requires electron-withdrawing groups on the aromatic substrate so that the intermediate is adequately stabilized.[9a-c] Consequently, the scope of this process is severely limited and probably will not extend to alkoxyaryl systems like that in mesembrine, since strongly electron-donating groups destabilize the negative charge of the Meisenheimer complex. The benzyne pathway requires a strong base for proton removal[10] and may not be very selective because of the high reactivity of the dehydrobenzene. For example, attempts to form arylacetonitriles have met with mixed results.[11] The amide base used to form the benzynes trapped much of the dehydroaromatic intermediates. The electron-transfer approach[12] seems to be limited to highly stabilized nucleophiles,[13] or systems where large excesses of the nucleophile can be tolerated (in particular, the anions of acetonitrile, acetone, and ammonia),[14a] or with very reactive dianions.[14b]

Our early attempts to arylate lactams met with few encouraging results. Bromobenzene and *N*-methylpyrrolidinone (NMP) in the presence of sodium amide in ammonia gave no α-phenyl lactam. Various base combinations, including $NaNH_2$/KH, $NaNH_2$/KO-*t*-Bu,[15] and $NaNH_2$/LDA, gave only traces of aryl lactam. α-Carboethoxy-NMP was prepared but failed to react with either bromobenzene or iodobenzene and $NaNH_2$ or lithium diisopropylamide (LDA), even when cuprous bromide or iodide was added.[13] One attempt with the carefully dried diazonium salt from anthranilic acid[16] also failed to give any of the desired α-aryl lactam. *N*-Carboethoxypyrrolidinone and *N*-benzoylpyrrolidinone also did not react with bromobenzene in the presence of excess LDA or lithium isopropylcyclohexylamide (LICA). Benzenechromium tricarbonyl[17] was recovered when stirred with NMP and excess LDA.[18]

Table I. Arylation of Lactams



R[a]	base (equiv)	ArBr[b]	% yield[c]
CH_3	LICA (3.2)	BB	35–40
CH_3 (4.0)	LICA (8.0)	BV	20
CH_3	LICA (4.0)	BD	16[d]
$CH_2C_6H_5$	LICA (4.0)	BB	24–27
$CH_2C_6H_5$	LICA (4.0)	BV	35
$CH_2C_6H_5$ (4.0)	LICA (8.0)	BV	40
CH_3	LDA (3.2)	BB	18
CH_3	LTMP (3.2)	BB	35[e]
CH_3	LDCA (4.0)	BB	30
$CH_2C_6H_5$	LICA (4.0)	BD	30
CH_3	LICA (4.0)	BA	50[f]

[a] Two equivalents of lactam used (based on ArBr), unless otherwise indicated. [b] Key: BB = bromobenzene, BV = bromoveratrole, BD = 4-bromo-1,2-(methylenedioxy)benzene, BA = 4-bromoanisole. [c] Refers to pure, isolated products, except as noted. [d] Material in purified yields up to 27% darken with time. [e] 3,3-Diphenyl-NMP also formed. [f] Both meta and para products obtained in a 1:1 ratio by GC/MS analysis.

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(3) For example, see the following: (a) Gassman, P. G.; Fox, B. L. *J. Org. Chem.* **1974**, *39*, 982. (b) Needles, H. L.; Whitfield, R. E. *Ibid.* **1966**, *31*, 989. (c) Trost, B. M.; Kunz, R. A. *Ibid.* **1974**, *39*, 2475. (d) Hullot, P.; Cuvigny, T.; Larcheveque, M.; Normant, H. *Can. J. Chem.* **1976**, *54*, 1098. See also ref 5.

(4) (a) α-Phenylcaprolactam was prepared in 10% yield by combining the methyl imino ether of caprolactam with the diazonium salt of anthranilic acid at 70 °C: Duong, T.; Prager, R. H.; Ward, A. D.; Kerr, D. I. B. *Aust. J. Chem.* **1976**, *29*, 2651. (b) Intramolecular arylation of amide enolates reportedly is photochemically induced: Goehring, R. R.; Sachdeva, Y. P.; Pisipati, J. S.; Sleevi, M. C.; Wolfe, J. F. *J. Am. Chem. Soc.* **1985**, *107*, 435.

(5) Several α-aryl lactams were prepared in low yields by combining caprolactams, amide bases, and *o*-chloroanisole: Bradley, G.; Cavalla, J. F.; Edington, T.; Shepherd, R. G.; White, A. C.; Bushell, B. J.; Johnson, J. R.; Weston, G. O. *Eur. J. Med. Chem.—Chim. Ther.* **1980**, *15*, 375. We thank Dr. Alan C. White for providing a copy of this manuscript.

(6) The importance of α-aryl ketones, esters, and nitriles can be seen by considering the diverse routes that have been developed for α-arylation of the corresponding substrates. Here are some of the ways by which enolates and equivalents have been arylated by electrophilic aryl species. (a) An enamine with a dinitrochloroaromatic: Kuehne, M. E. *J. Am. Chem. Soc.* **1962**, *84*, 837. (b) Haloaromatics plus ketones and strong base: Kametani, T.; Noguchi, S.; Agata, I.; Aono, T.; Kigasawa, K.; Hiiragi, M.; Hayasaka, T.; Kusawa, O. *J. Chem. Soc. C* **1971**, 1047. Kametani, T.; Kigasawa, K.; Hiiragi, M.; Hayasaka, T.; Kusama, O. *Ibid.* **1971**, 1051. Caubere, P.; Guillaumet, G.; Mourad, M. S. *Tetrahedron* **1973**, *29*, 1857. Gregoire, B.; Carre, M.-C.; Caubere, P. *J. Org. Chem.* **1986**, *51*, 1419. (c) Aryl iodides plus cyanoacetates and base with Pd^{2+}: Uno, M.; Seto, K.; Ueda, W.; Masuda, M.; Takahashi, S. *Synthesis* **1985**, 506. (d) Enol silyl ethers and acetates plus aryldiazonium salts: Sakakura, T.; Hara, M.; Tanaka, M. *J. Chem. Soc., Chem. Commun.* **1985**, 1545. Allard, M.; Levisalles, J. *Bull. Soc. Chim. Fr.* **1972**, 1926. (e) Enol silyl ethers and aryl halides plus Pd^{2+} and a tin fluoride: Kuwajima, I.; Urabe, H. *J. Am. Chem. Soc.* **1982**, *104*, 6831 and references cited therein. (f) Lithium, zinc, and tin ester enolates plus aryl halides with Pd^{2+}, Ni^{2+}, or phosphines: Fauvarque, J. F.; Jutand, A. *J. Organomet. Chem.* **1977**, *132*, C17. Millard, A. A.; Rathke, M. W. *J. Am. Chem. Soc.* **1977**, *99*, 4833. Kosugi, M.; Negishi, Y.; Kameyama, M.; Migita, T. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3383.

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(8) Intramolecular arylation of ketones and esters has been used as the key step in the synthesis of various alkaloids. For example, see the following: Julia, M.; Le Goffic, F.; Igolen, J.; Baillarge, M. *Tetrahedron Lett.* **1969**, 1569. Semmelhack, M. F.; Chong, B. P.; Stauffer, R. D.; Rogerson, T. D.; Chong, A.; Jones, L. D. *J. Am. Chem. Soc.* **1975**, *97*, 2507. Osuka, A.; Mori, Y.; Suzuki, H. *Chem. Lett.* **1982**, 2031.

(9) (a) Bunnett, J. F.; Zahler, R. E. *Chem. Rev.* **1951**, *49*, 273. (b) Bunnett, J. F. *Acc. Chem. Res.* **1972**, *5*, 139. (c) deVargas, E. B.; de Rossi, R. H.; Veglia, A. V. *J. Org. Chem.* **1986**, *51*, 1976. (d) The reaction of organometallics with 2-(*o*-methoxyaryl)oxazolines is reviewed in: Reuman, M.; Meyers, A. I. *Tetrahedron* **1985**, *41*, 837.

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(15) This is a potent metalating combination: Essiz, M.; Guillaumet, G.; Brunet, J.-J.; Caubere, P. *J. Org. Chem.* **1980**, *45*, 240.

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Success came from the reaction of dialkylamide bases, lactams, and aryl bromides[19] at temperatures of 0–30 °C. For example, 1-methyl-3-phenyl-2-pyrrolidinone is obtained in 35–40% yields by allowing 3.2 equiv of LICA to react with 2.0 equiv of NMP and 1.0 equiv of bromobenzene at 20 °C. Similarly, bromoveratrole (1.0 equiv) leads to a 30% yield of the α-(3,4-dimethoxyphenyl) lactam when stirred with 4.0 equiv of NMP and 8.0 equiv of LICA. 1-Benzyl-2-pyrrolidinone (NBP; 2.0 equiv) reacts with LICA (4.0 equiv) and bromoveratrole (1.0 equiv) to give a 35% yield of α-aryl lactam. Using half as much bromoveratrole raises the yield to 40%. This NBP system is particularly convenient, because partial water solubility of the product is not a problem as with the products derived from NMP. A summary of all systems is given in Table I.

Different dialkylamide bases were tried to bring about this conversion. LICA seems to be the best as judged by the yield of aryl lactam and the amount of side products (mainly the dialkylanilines derived from the aryl bromide). By comparison, LDA promotes an 18% yield of α-phenyl-NMP. Lithium 2,2,6,6-tetramethylpiperidide (LTMP)[20] permits a 35% isolated yield of α-phenyl-NMP, but another 3% or so of the diaryl lactam is also present when the crude product mixture is analyzed by GC/MS. No substituted aniline is formed in this latter reaction. The somewhat less expensive lithium dicyclohexylamide (LDCA) leads to a 30% yield of α-phenyl-NMP. Some dicyclohexylaniline was detected when the crude product was analyzed by GC/MS. No aryl lactam was formed when lithium hexamethyldisilazide was used. Bromobenzene was recovered.

Temperature is very critical for successful arylation. Low temperatures (−78 °C) are not high enough to allow the formation of any aryl lactam. Low yields of product are possible at intermediate temperatures (up to −20 °C). Elevated temperatures (50–60 °C) apparently cause condensation of the lactam, while 0–30 °C seems optimal.

The mechanism of this substitution reaction apparently involves benzyne intermediates. This is not clear from the results with bromoveratrole where only the 4-substituted veratrole is isolated; however, this same result is observed under aryne-forming conditions with this system.[11b] A small amount (ca. 5%) of a regioisomer is sometimes seen in the corresponding methylenedioxy system, and this is highly suggestive of a benzyne intermediate. Even more compelling evidence is the formation of two products in equal amounts from the reaction of *p*-bromoanisole with NMP and excess LICA.[21]

Experimental Section

All reactions requiring anhydrous conditions were performed under nitrogen in oven- and flame-dried glassware. Tetrahydrofuran (THF) was distilled from potassium shortly before use. Dry ether was distilled from lithium aluminum hydride. All reagents and other solvents from commercial sources were used without further purification.

Proton NMR spectra (60 MHz) were recorded on a Varian EM-360 spectrometer. Both 90-MHz ^{1}H and ^{13}C NMR spectra were obtained on a JEOL FX-90Q instrument. Chemical shifts are reported in parts per million (ppm) vs. tetramethylsilane as an internal standard. Infrared (IR) spectra were recorded on a Perkin-Elmer 137 or 1310 spectrophotometer with the 1601-cm^{-1} polystyrene peak used for calibration. Mass spectra were obtained on a Finnigan 4021-C GC/MS in the electron impact (EI) mode with an ionizing power of 70 eV. Small-scale distillations were done with a Buchi Kugelrohr apparatus, and the boiling points are uncorrected. Melting points were taken on a Mel-Temp apparatus and are uncorrected.

Preparation of 1-Methyl-3-phenyl-2-pyrrolidinone. Cyclohexylisopropylamine (4.52 g, 32.0 mmol) was dissolved in 30 mL of THF at −78°C, and 32.0 mmol of *n*-BuLi/hexane was added via syringe. After 20 min, the cold bath was removed, and the flask was allowed to warm up to about 0 °C over 20 min. The flask was again cooled to −78 °C, and 1.98 g (20.0 mmol) of NMP in 5 mL of THF was added dropwise over 2–4 min. This light yellow solution was stirred for 1 h (longer time does not affect the yield). The cold bath was removed, and the flask was allowed to warm unassisted to 20 °C when 1.57 g (10.0 mmol) of bromobenzene in 10 mL of THF was added dropwise over 5 min. This gave a deep red solution that was stirred overnight at room temperature and then was quenched with a mixture of 50 mL each of ether and water. About 200 mL of 10% HCl was added, followed by enough sodium chloride to saturate the aqueous layer. Extraction with four 50-mL portions of ether gave, after concentration, 1.75 g of light yellow oil. Purification (that same day to avoid a reduction in yield by about 5%) by chromatography on silica gel (1.5 × 70 cm) using ethyl acetate as eluent gave 0.70 g (40%) of pure product that crystallized upon standing: mp 58–59 °C [lit. mp 58–59 °C,[22a] 60–61 °C;[22b] bp 140–145 °C (0.5 mm)];[23] ^{1}H NMR ($CDCl_3$) δ 1.80–2.72 (m, 2 H), 2.93 (s, 3 H), 3.36–3.65 (m, 3 H), 7.26 (s, 5 H); ^{13}C NMR ($CDCl_3$) δ 27.95, 30.67, 47.73, 48.00, 126.93, 127.85, 128.66, 139.99, 174.93; IR (NaCl) 3010, 2940, 1685, 1600, 1490, 1445, 1430, 1390, 1290, 1100, 1025, 920, 725, 695 cm^{-1}; GC/MS, *m/e* (rel abund) 175 (P, 48), 117 (100), 42 (30).

Preparation of 1-Methyl-3-(3,4-dimethoxyphenyl)-2-pyrrolidinone. LICA was prepared from 20.2 mmol of *n*-BuLi and 20.8 mmol of amine in 20 mL of THF and was cooled to −78 °C as NMP (0.99 g, 10.0 mmol) in 5 mL of THF was added dropwise over 10 min. After 45 min, the reaction mixture was allowed to warm to about 10 °C, and bromoveratrole (0.54 g, 2.50 mmol) in 5 mL of THF was added over 1–2 min. The dark reaction mixture was allowed to stir at room temperature for 12 h before being quenched with 50 mL of a 1:1 mixture of ether and 4 N HCl. The aqueous layer was saturated with NaCl and extracted with four 60-mL portions of ether to give, after concentration, 0.28 g of dark liquid. Chromatography on silica gel (2 × 20 cm) gave 0.12 g (20%) of pure α-aryl lactam after elution of veratrole: ^{1}H NMR ($CDCl_3$) δ 1.8–2.8 (m, 2 H), 2.91 (s, 3 H), 3.3–3.7 (m, 3 H), 3.84 (s, 3 H), 3.87 (s, 3 H), 6.80 (br s, 3 H); ^{13}C NMR δ 27.79, 30.01, 47.35, 47.67, 56.45 (2 C), 113.01 (2 C), 120.21, 133.16, 148.92, 149.96, 174.82; IR (NaCl) 2965, 2885, 1680, 1600, 1625, 1505, 1450, 1390, 1280, 1245, 1220, 1140, 1135, 1090, 1020, 925, 850, 760, 700 cm^{-1}; GC/MS, *m/e* (rel abund) 235 (P, 100), 178 (35), 163 (42), 147 (28), 107 (30), 97 (60), 91 (33), 42 (80).

Preparation of 1-Methyl-3-[3,4-(methylenedioxy)-phenyl]-2-pyrrolidinone. The usual procedure gave 1.42 g of a brown oil, which was purified by chromatography on silica gel using ethyl acetate. The desired product (0.09 g, 16%) was analyzed as follows: ^{1}H NMR ($CDCl_3$) δ 1.8–2.7 (m, 1 H), 2.92 (s, 3 H), 3.3–3.65 (m, 3 H), 5.91 (s, 2 H), 6.71 (br s, 3 H); ^{13}C NMR ($CDCl_3$) δ 28.06, 30.12, 47.67, 47.78, 100.98, 108.35, 121.13, 121.84, 133.79, 146.60, 147.95, 175.04; IR (NaCl) 2975, 1680, 1605, 1495, 1430, 1395, 1350, 1280, 1240, 1030, 925, 810, 705 cm^{-1}; GC/MS, *m/e* (rel abund) 219 (P, 100), 162 (78), 148 (36), 147 (39), 132 (43), 131 (62), 104 (75), 42 (33).

Preparation of 1-Benzyl-3-phenyl-2-pyrrolidinone. The usual procedure gave 1.91 g of crude product, which was purified by chromatography on silica gel (1.8 × 40 cm) using 3:1 ether/hexane as the eluent. A light yellow oil (0.62 g, 27%) was obtained:

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(23) Vacuum distillation alone is not adequate to purify this product. Within several days, a distilled (only) product will turn deep blue or purple. Crude, undistilled product does this within 1 day of initial isolation. Chromatographed material is stable indefinitely.

^{1}H NMR ($CDCl_3$) δ 1.9–2.8 (m, 2 H), 3.29 (m, 2 H), 3.68 (t, J = 8.6 Hz, 1H), 4.50 (q_{AB}, J_A = 14.8 Hz, J_B = 17.9 Hz, 2 H), 7.27 (br s, 10 H); ^{13}C NMR ($CDCl_3$) δ 27.74, 45.02, 47.29, 48.11, 125.25, 126.93, 127.64, 127.91, 128.34, 128.72, 136.95, 140.15, 174.55; IR (NaCl) 3060, 3040, 2930, 2880, 1690, 1604, 1500, 1460, 1430, 1360, 1290, 760, 710 cm^{-1}; GC/MS, m/e (rel abund) 251 (P, 27), 118 (30), 91 (100).

Preparation of 1-Benzyl-3-(3,4-dimethoxyphenyl)-2-pyrrolidinone. The usual procedure gave 1.8 g of crude product. Distillation gave veratrole as a first fraction, NBP as a second fraction, and the desired product (0.54 g, 35%) as a third fraction: bp 235–245 °C (0.5 mm); ^{1}H NMR ($CDCl_3$) δ 1.8–2.7 (m, 2 H), 3.2–3.7 (m, 3 H), 3.85 (s, 6 H), 4.52 (q_{AB}, J_A = 14.5 Hz, J_B = 18.0 Hz, 2 H), 4.52 (m, 2 H), 6.80 (br s, 3 H), 7.30 (s, 5 H); ^{13}C NMR ($CDCl_3$) δ 27.74, 44.91, 47.13, 47.62, 55.91, 56.02, 111.44, 111.65, 119.83, 127.64, 128.28, 128.72, 132.51, 136.63, 148.22, 149.25, 174.82; IR (NaCl) 2965, 1675, 1600, 1585, 1505, 1480, 1445, 1425, 1345, 1320, 1245, 1135, 1075, 1020, 930, 760, 730, 695 cm^{-1}; GC/MS, m/e (rel abund) 311 (P, 70), 164 (35), 151 (40), 91 (100).

Preparation of 1-Benzyl-3-[3,4-(methylenedioxy)-phenyl]-2-pyrrolidinone. The usual procedure gave a crude product, which was distilled. The first fraction was mainly unreacted NBP, while the desired product (0.21 g, 27%) was obtained as a second fraction: bp 230–240 °C (0.5 mm); ^{1}H NMR ($CDCl_3$) δ 1.8–2.6 (m, 2 H), 3.3 (m, 2 H), 3.64 (t, J = 8.8 Hz, 1 H), 4.51 (m, 2 H), 5.92 (s, 2 H), 6.74 (br s, 3 H), 7.30 (s, 5 H); ^{13}C NMR ($CDCl_3$) δ 27.95, 44.80, 47.13, 47.89, 100.98, 108.29, 108.40, 121.13, 127.64, 128.23, 128.72, 133.65, 136.57, 146.65, 148.00, 174.71; IR (NaCl) 2915, 1675, 1605, 1480, 1430, 1345, 1270, 1240, 1185, 1120, 1100, 1075, 1030, 930, 860, 810, 780, 740, 700 cm^{-1}; GC/MS, m/e (rel abund) 295 (P, 91), 204 (46), 162 (60), 148 (51), 135 (90), 91 (100).

Reaction of *p*-Bromoanisole with NMP. The usual procedure gave 0.85 g of dark oil. Chromatography on silica gel (2 × 20 cm) first gave nonpolar impurities followed by an aryl lactam fraction (0.53 g, 51%) as a yellow oil. Analysis by GC/MS showed two isomers in a 1:1 ratio having identical fragmentation patterns: GC/MS, m/e (rel abund) 205 (P, 100), 148 (60), 117 (30), 42 (60); ^{1}H NMR ($CDCl_3$) δ 1.8–2.7 (m, 2 H), 2.90 (s, 3 H), 3.2–3.65 (m, 3 H), 3.76 (s, $^3/_2$ H), 3.77 (s, $^3/_2$ H), 6.65–7.30 (m, 4 H); IR (NaCl) 2965, 2900, 1675, 1605, 1580, 1505, 1445, 1430, 1395, 1290, 1240, 1175, 1150, 1030, 780 cm^{-1}.

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Communications

Regiospecificity in the Alkylation of Ester Enolates: Synthesis of Sterically Hindered Diarylketene Acetals

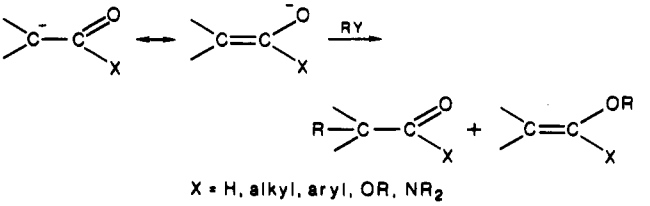
Summary: The alkylation of the enolates of methyl bis(pentamethylphenyl)acetate and of isopropyl bis(pentachlorophenyl)acetate occurs exclusively on oxygen to yield the diarylketene acetals; the extreme steric hindrance of these groups is also responsible for the stability of these ketene acetals in acid.

Sir: The alkylation of enolate anions (conjugate bases of aldehydes, ketones, esters, amides) may in principle occur on either carbon or oxygen (Scheme I).[1] The actual regiospecificity depends strongly on solvent, temperature, and counterion.[2]

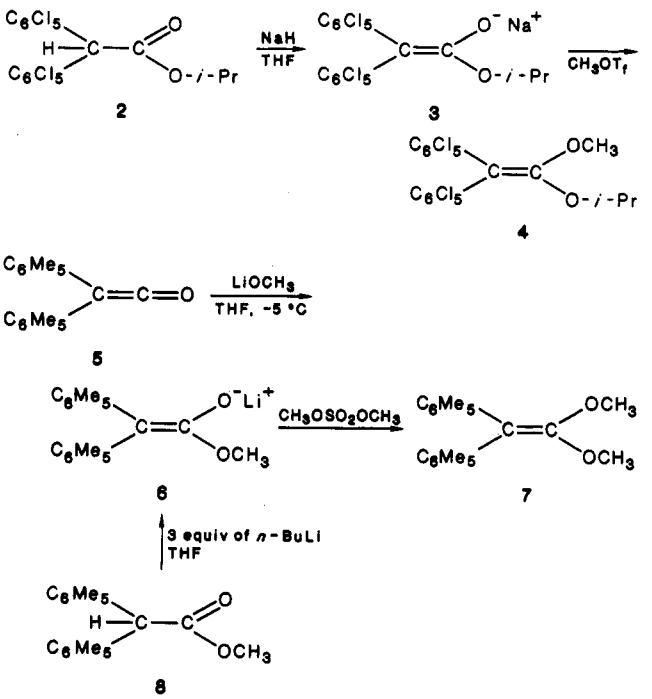
Alkylation of preformed enolates of aldehydes and ketones occurs exclusively on the carbon[3] in less polar solvents. The use of more polar solvents such as Me_2SO and HMPT increases the extent of O-alkylation.[4]

Tidwell[5] has investigated the alkylation of crowded Li enolates of aldehydes and ketones such as 1,1-di-*tert*-butylacetone and 1,1-di-*tert*-butyl-3,3,3-trimethylacetone and found C-alkylation only in the former and mixtures of O and C in the latter. It is interesting to note that in this case extreme steric hindrance with bulky alkyl groups does not afford regioselectivity; this may be related to the high strain energy resulting from interaction between adjacent *tert*-butyl groups.[6]

Scheme I



Scheme II



On the other hand, the alkylation of enolates of carboxylic acid derivatives is virtually always exclusively on

(1) For a review on factors affecting O vs. C alkylation of enolates, see: Barton, D.; Ollis, W. O. *Comprehensive Organic Chemistry*; Pergamon: New York, 1979; Vol. 1, p 1032 ff and references cited therein.
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